

09/673160

529 Rec'd PCT/PTC 10 OCT2000

Claims

1. An ultrasound contrast agent comprising an injectable oil-in-water emulsion wherein there are heterogeneous gas-containing nucleation sites associated with droplets of the dispersed oil phase.

2. A contrast agent as claimed in claim 1 wherein the nucleation sites are present within dispersed oil phase droplets.

3. A contrast agent as claimed in claim 2 wherein the nucleation sites comprise free gas microbubbles, surfactant- or lipid-stabilised gas microbubbles, polymer- or protein-encapsulated gas microbubbles, gas-containing porous solid microparticles, gas-containing rough-surfaced solid microparticles, gas-containing polymeric microparticles, or gas-containing fullerenes, clathrates or nanotubes.

4. A contrast agent as claimed in claim 1 wherein nucleation sites are present within membranes stabilising the dispersed oil phase droplets or in contact with the outside of such membranes.

claim 1
5. A contrast agent as claimed in ~~any of the preceding claims~~ wherein the oil phase comprises one or more components selected from aliphatic ethers, polycyclic oils and alcohols, heterocyclic compounds, aliphatic hydrocarbons, cycloaliphatic hydrocarbons and halogenated hydrocarbons, said component(s) having a boiling point not exceeding 60°C.

6. A contrast agent as claimed in claim 5 wherein the oil phase comprises one or more perfluorocarbons.

09673160-12100

7. A contrast agent as claimed in claim 6 wherein said perfluorocarbon is selected from perfluorobutanes, perfluoropentanes, perfluorohexanes, perfluorocyclobutane, perfluorodimethylcyclobutanes, perfluorocyclopentane, perfluoromethylcyclopentane, perfluorobutenes, perfluorobutadienes, perfluoropentenes, perfluorohexenes, perfluorocyclopentene, perfluorocyclopentadiene and perfluoro-t-butanol.
8. A contrast agent as claimed in ^{claim 1} ~~any of the preceding claims~~ wherein the oil phase contains a gaseous solute.
9. A contrast agent as claimed in claim 8 wherein the oil phase comprises air, oxygen or carbon dioxide dissolved in a liquid fluorocarbon.
10. A contrast agent as claimed in ^{claim 1} ~~any of the preceding claims~~ wherein the dispersed oil phase droplets are stabilised by a surfactant selected from fatty acids, carbohydrate and triglyceride esters of fatty acids, phospholipids, proteins, block copolymer surfactants, fluorine-containing surfactants and cationic surfactants.
11. A contrast agent as claimed in ^{claim 1} ~~any of claims 1 to 9~~ wherein the dispersed oil phase droplets are stabilised by polymeric wall-forming encapsulating material or by incorporation into porous latex particles.
12. A contrast agent as claimed in ^{claim 1} ~~any of the preceding claims~~ wherein the oil phase has a boiling point not exceeding 42°C.
13. A combined preparation for simultaneous, separate or sequential use as a contrast agent in ultrasound imaging, said preparation comprising:

- 23 -

i) a contrast agent as claimed in any of the preceding claims, and

ii) a vasodilator drug.

5 14. A combined preparation as claimed in claim 13 wherein said vasodilator drug is adenosine.

a 15. A drug delivery agent comprising a contrast agent
10 as claimed in ~~any of claims 1 to 12~~^{claim 1} together with a therapeutic drug.

15 16. A drug delivery agent as claimed in claim 15 wherein a hydrophobic drug is dissolved in the oil phase.

17. A drug delivery agent as claimed in claim 15 wherein the drug is present as nano- or micro-sized particles.

20 18. A method of generating enhanced images of a human or non-human animal subject which comprises the steps of
a injecting a contrast agent as claimed in ~~any of claims 1 to 14~~^{claim 1} into the vascular system of said subject and
1 generating an ultrasound image of at least a part of
25 said subject.

19. A method as claimed in claim 18 wherein microbubble growth from the contrast agent is activated within the subject by application of external activation.

30

20. A method as claimed in claim 19 wherein said external activation comprises ultrasound irradiation.

a 21. Use of a contrast agent as claimed in ~~any of claims 1 to 12~~^{claim 1} in ultrasound therapy.
a 35

09673460-121100

- 24 -

22. Use as claimed in claim 21 wherein said therapy involves cell killing ~~or~~ blocking of blood flow to a site of interest.

09673160.121100